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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 02/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/058,566	ALBERTSEN ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *1-34 and 41-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-40 and 46-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group III (claims 35-36 and 38-55 and SEQ ID NO:5) in the response filed 8 October 2003 is acknowledged. The traversal is on the ground(s) that the claims of Group III are drawn to the BS92-7 promoter and methods of its use, while the claims of Group I are drawn to the BS92-7 gene. Applicant urges that an independent search of the sequences is thus not necessary. This is not found persuasive because the inventions are related as combination and subcombination and the subcombination has utility by itself or in other combinations. In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the subcombinations have different promoters or exogenous sequences. Thus, the searches are not coextensive.

The traversal is on the ground(s) that separation of claims to the gene in Group I from claim 34 to the deposited seed [sic] containing the gene. This is not found persuasive. The restriction was made because nowhere does the specification state what is in ATCC deposit no. 98932.

Group V (claims 37 and 56-57) will be examined along with Group III and the restriction between those two groups is withdrawn.

Claims 41-45 are drawn to a non-elected sequence and are withdrawn from consideration as being drawn to non-elected inventions, as are claims 1-34.

Claims 35-40 and 46-57 are examined to the extent they read on SEQ ID NOs:5 or 6.

The requirement is still deemed proper and is therefore made FINAL.

2. The substitute specification filed 21 May 2002 was not entered because it does not contain the preliminary amendment filed with the application (the priority information).

3. If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from either the legend or the Brief Description of Figure 6.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth herein. Failure to fully comply with both of these requirements in the time period set forth in this Office action will be held to be non-responsive.

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because the specification to which the oath or declaration is directed has not been adequately identified. See MPEP § 601.01(a).

6. The abstract is not descriptive of the instant invention, which is XXXXXXX. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

7. The title of the invention is not descriptive of the instant invention, as above. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

Claim Objections

8. Claims 36, 38-39, 48-49, 51-54 and 56-57 are objected to because of the following informalities:

In claim 36, "NO." should be replaced with --NO:--.

In claims 38, "Seq. ID. NO." should be replaced with --SEQ ID NO:--.

In claim 39, line 2, "No." should be replaced with --NO:-- in line 3, "ID. NO." should be replaced with --ID NO:--, and in line 4 "Seq. ID. Nos." should be replaced with --SEQ ID NOs:--.

In claims 48-49, 52-54 and 57, line 1, and in claims 39 and 51, line 2, a comma should be inserted before "wherein".

Claim 48, line 2, is missing a comma after "BS92-7".

In claim 48, "from any one" should be replaced with --from the group consisting--.

In claim 52, there should be a comma after the first "plant" in line 2, and there should be an article before "function" in line 1.

In claim 56, line 5, --and-- should be inserted after "fertile;".

In claim 57, "further comprising" should be replaced with --wherein the method further comprises--.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claim 37-38 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to regulatory regions, which are products of nature.

Claims 37-38, as written, do not sufficiently distinguish over nucleic acids as they exist in nature because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). It is suggested that the claims be modified to refer to the

hand of the inventor, *e.g.* by replacing "A" in claims 37-38 with --An isolated--. See MPEP 2105.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 35-37, 39-40 and 46-57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for promoters of SEQ ID NO:5 or 6 and certain methods of their use, does not reasonably provide enablement for a multitude of nucleic acids that hybridize to SEQ ID NO:5 or that are essential for the transcription of the BS92-7 gene, and methods of their use. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a multitude of nucleic acids that hybridize to SEQ ID NO:5 or that are essential for the transcription of the BS92-7 gene (that is, any regulatory region), wherein the nucleic acids are from any source, and methods of their use.

The instant specification, however, only provides guidance for identification of an individual, BS92-7, of a maize Mu population that is male sterile because of the Mu event (example 1); identification of genomic and cDNA clones, SEQ ID NOs:3 and 1, respectively, of the wild type DNA corresponding to one event (examples 2-4); cloning the male-tissue specific promoter of the gene and identification of an essential region, SEQ ID NOs:5 and 6, respectively

(example 5), and use of the promoter to drive expression of cytotoxic genes and confer male sterile on a plant (example 7); mapping of the BS97-7 gene to show it is allelic to ms7 (examples 8-9); and identification of a DNA from sorghum that can be amplified using primers based on the BS92-7 sequence (example 10).

The instant specification fails to provide guidance for a multitude of nucleic acids that hybridize to SEQ ID NO:5 or that are essential for the transcription of the BS92-7 gene (that is, any regulatory region), wherein the nucleic acids are from any source, and methods of their use.

The specification also fails to provide guidance for a method of mediating male fertility in a plant, wherein a plant is transformed with a construct comprising an male-tissue specific promoter operably linked to an exogenous coding sequence, resulting in the production of a plant that is constitutively male sterile and inducibly fertile.

The specification also fails to teach any 130 nucleotide long region upstream of the TATA box of the BS97-2 gene that is male-tissue specific regulatory region.

Mutation of promoter sequences produces unpredictable results. Donald et al (1990, EMBO J. 9:1717-1726) in a mutational analysis of the *Arabidopsis rbcS-1A* promoter found that the effect of a particular mutation was dependent on promoter fragment length (paragraph spanning pg 1723-1724).

Prediction of promoter sequences required for tissue-specificity is also unpredictable. Eyal et al (1995, Plant Cell 7:373-384) located pollen specificity to 30 bp long regions of two tomato promoters (paragraph spanning the columns on pg 377), but the sequence thought to play an essential role in that specificity (pg 381, right column, paragraph 3) is not present in the pollen-preferred promoter of the instant application.

Identification of the functional parts of promoters is unpredictable. Chen et al (2000, Sex. Plant Reprod. 13:85-94) teach that two promoters with similar expression patterns have major differences in the expression elements required for expression in various flower parts (pg 92, right column, last two paragraphs).

The region of a given promoter that has a specific activity cannot be predicted and involves the complex interaction of different subdomains (Benfrey et al, 1990, Science 250:959-966, see Abstract, Fig. 3-5). Even a very small region may be critical for activity, and the criticality of a particular region must be determined empirically (Kim et al, 1994, Plant Mol. Biol. 24:105-117, Tables 1-4, Abstract, Fig. 1-2).

As the specification does not describe the transformation of any plant with a comprising a 130 nucleotide region upstream of the TATA box of the BS97-2 gene that is male-tissue specific regulatory region, that hybridizes to SEQ ID NO:5 or that is essential for the transcription of the BS92-7 gene, operably linked to an exogenous gene , undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with expression of the exogenous gene, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

13. Claims 35-37, 39-40 and 46-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of nucleic acids that hybridize to SEQ ID NO:5 or that are essential for the transcription of the BS92-7 gene (that is, any regulatory region), wherein the nucleic acids are from any source. In contrast, the specification only describes a promoter from maize that comprises SEQ ID NO:5 and 6. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described nucleic acids that hybridize to SEQ ID NO:5 or that are essential for the transcription of the BS92-7 gene within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 35-37, 39-40 and 46-57 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claim 35 is indefinite in its recitation of "encoding the promoter region", as promoters are not encoded.

Claims 36 and 39 are indefinite in their recitation of "conditions of high stringency". It is unclear what those conditions are; thus, the metes and bounds of the claimed nucleic acid are unclear.

Claims 37 and 56 are indefinite in their recitation of "essential for imitating transcription of the BS92-7 gene." Claim 39 is similarly indefinite in its recitation of "essential for imitating transcription of SEQ ID Nos.1, 3 or 7." It is not clear if applicant is referring to the essential region of the promoter of the BS92-7 gene or if Applicant is referring to any promoter, which would be essential for initiating any gene. For purposes of examination, the latter interpretation was used.

Claim 40 is indefinite in its recitation of "comprising nucleotide sequences of about 130 contiguous basepairs upstream of the TATA box of the BS92-7 gene". It is not clear of the region is 130 nucleotides long and located anywhere on the chromosome as long as it is a promoter and as long as it is "upstream" of the TATA box of the BS97-2 gene or if the region starts 130 nucleotides upstream of the TATA box of the BS92-7 gene.

Claim 46 lacks antecedent basis for the limitation "the male tissue specific regulatory element of claim 37" as claim 37 is drawn to a male tissue-preferred regulatory region.

In claim 47 it is not clear where the promoter of the expression vector is located relative to the promoter of the exogenous gene. It is noted that "gene" implies an open reading frame as well as all the regulatory sequences associated with it.

Claim 48 is indefinite in its recitation of "promoter is ... CaMV 35S, SGB6, BS92-7 MS45 or 5126" as these are not promoters but genes.

In claim 51 it is unclear what the phrase following "comprising" is intended to modify. - plant? Method? By position in the claim it modifies "plant".

Claim 51 lacks antecedent basis for the limitations "the exogenous gene" in line 2 and "the regulatory element in conjunction with the promoter" in line 3. Additionally, "control" should be plural.

Claim 51 is indefinite in its recitation of "impacting male fertility". Virtually any gene affects male fertility in some way - for example a gene responsible for seed germination impacts male fertility of the plant grown from the seed because without germination of the seed, the plant could not be male fertile. It is not clear what the exogenous gene does. Claim 52 is similarly indefinite is nits recitation of "disrupts function of male tissue".

Claim 53 is indefinite in its recitation of "(?)" to modify "regulatory". It is unclear what this symbol is intended to mean.

Claim 55 lacks antecedent basis for the limitations " the male sterile plant" in line 1 and "the second gene" in line 3.

Claims 56-57 provide for the production of second and fourth parent plants, respectively, but do not set forth any active, positive steps involved in the method. The starting materials and method steps of the process are unclear.

16. Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are an inducible promoter/regulatory element.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 36-37, 39, 46-53 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Tunen et al (1999, US Patent 6,005,167).

Van Tunen et al teach a method for mediating male fertility in a plant comprising introducing into a plant an expression vector comprising an exogenous gene operably linked to a promoter operably linked to a male-tissue specific regulatory region, wherein the promoter is the 35S promoter and the male-tissue specific regulatory region is the CIS-A anther box (claims 6-7, 26-27 and 32-33). The male-tissue specific regulatory region would inherently be essential for initiating transcription of the BS92-7 gene because any promoter would be so essential; additionally it would hybridize to SEQ ID NO:5 or 6 under conditions of "high stringency". The regulatory element in conjunction with the promoter would be inducible because the combination results in tissue-specific expression. Van Tunen et al also teach crossing the plants produced by this method with male fertile plants (column 14, lines 42-44).

19. Claims 36-37, 39, 46-47, 49-53 and 55-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Hodges et al (1999, US Patent 5,929,307).

Hodges et al teach a method for mediating male fertility in a plant comprising introducing into a plant an expression vector comprising an exogenous gene operably linked to a core promoter operably linked to a male-tissue specific regulatory region (claims 1-24). The male-

tissue specific regulatory region would inherently be essential for initiating transcription of the BS92-7 gene because any promoter would be so essential; additionally it would hybridize to SEQ ID NO:5 or 6 under conditions of "high stringency". The regulatory element in conjunction with the promoter would be inducible because the combination results in tissue-specific expression. Hodges et al also teach crossing the plants produced by this method with male fertile plants (claims 19 and 21).

20. Claims 36-37, 39-40, 46-54 and 56-57 are rejected under 35 U.S.C. 102(b) as being anticipated by Albertsen et al (1999, US Patent 5,859,341).

Albertsen et al teach a method for mediating male fertility wherein a plant is transformed with a construct comprising an inducible promoter operably linked to an exogenous coding sequence, resulting in the production of a plant that is constitutively male sterile and inducibly fertile and crossing the resulting plants through several generations (claims 1-11). The promoter would inherently be essential for initiating transcription of the BS92-7 gene because any promoter would be so essential.

21. Claim 38 is free of the prior art, given the failure of the prior art to teach or suggest an isolated nucleic acid of SEQ ID NO:6. To the extent it reads on a region that starts 130 nucleotides upstream of the TATA box of the BS92-7 gene, claim 40 is free of the prior art because that regions is comprised within SEQ ID NO:6.

22. Claim 38 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.

Conclusion

23. No claim is allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
December 23, 2003